

10/541362

JC20 Rec'd PCT/PTO 06 JUL 2005

**THE FOLLOWING ARE THE ENGLISH TRANSLATION
OF ANNEXES TO THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT (ARTICLE 34):**

Amended Sheets (Pages 30-34)

CLAIMS AS AMENDED

1. A polymer-based injectable gel-forming composition for intratissue and/or intravascular implantation, characterized in that it comprises:
- 5 - at least one linear polymer that is water-insoluble and soluble in at least one water-miscible solvent,
- at least one water-insoluble, hydrophilic crosslinked polymer, and
- 10 - at least one biocompatible, water-miscible solvent; and in that it is in the form of a suspension of particles of said hydrophilic crosslinked polymer in a solution of said linear polymer.
- 15 2. The injectable gel-forming composition as claimed in claim 1, characterized in that the linear polymer(s) is (are) chosen from poly(alkyl acrylates), poly(alkyl methacrylates), poly(alkyl cyanoacrylates), poly(vinyl acetates), poly(vinyl butyrates), poly(vinyl formals),
- 20 poly(vinyl acetals), poly(vinyl butyrals), polyoxypropylenes, polyoxytetramethylenes, water-insoluble cellulose esters, water-insoluble esters of chitosan or other polysaccharides, polylactides, polyglycolides, polycaprolactone, poly(malic acid) esters, poly(maleic acid) esters, poly(fumaric acid) esters, and water-
- 25 insoluble linear copolymers or derivatives comprising these compounds.
3. The injectable gel-forming composition as claimed in claim 2, characterized in that the linear polymer(s) is (are) chosen from poly(hydroxyethyl methacrylate), poly(methyl methacrylate), poly(hydroxypropyl meth-
- 30 acrylate), copolymers of hydroxyethyl methacrylate or hydroxypropyl methacrylate and of acrylonitrile, copolymers of hydroxyethyl methacrylate or hydroxy-
- 35 propyl methacrylate and of N-tert-butylacrylamide, copolymers of hydroxyethyl methacrylate or hydroxypropyl methacrylate and of acetoacetoxyethyl methacrylate, poly(N-acryloyl-2-amino-2-hydroxymethyl-1,3-

propanediol), poly(n-2-hydroxypropyl methacrylamide), and derivatives thereof.

4. The injectable gel-forming composition as claimed
5 in claim 3, characterized in that the linear polymer(s)
is (are) chosen from copolymers of hydroxypropyl
methacrylate and of acrylonitrile, copolymers of
hydroxypropyl methacrylate and of N-tert-
butylacrylamide and copolymers of hydroxypropyl
10 methacrylate and of acetoacetoxyethyl methacrylate.

5. The injectable gel-forming composition as claimed
in any one of the preceding claims, characterized in
that the linear polymer(s) represent(s) from 3 to 25%
15 (m/V).

6. The injectable gel-forming composition as claimed
in any one of the preceding claims, characterized in
that the hydrophilic crosslinked polymer(s) is (are)
20 chosen from the polymers derived from the crosslinking
of the water-insoluble linear polymers as defined in
claim 2.

7. The injectable gel-forming composition as claimed
25 in any one of claims 1 to 5, characterized in that the
hydrophilic crosslinked polymer(s) is (are) chosen from
the polymers derived from the crosslinking of water-
soluble linear polymers.

30 8. The injectable gel-forming composition as claimed
in claim 7, characterized in that the water-soluble
linear polymers are chosen from alginates; starch
derivatives; cellulose ethers; cellulose acetates with
a degree of substitution of between 0.6 and 0.8;
35 cellulose sulfates; water-soluble polysaccharides;
chitosan salts; acrylic and methacrylic polymers;
substituted or unsubstituted polyacrylamides and
polymethacrylamides; hydrolyzed derivatives of
poly(vinyl acetates); polymers derived from

polyoxyethylene, polyethyleneimine; soluble salts of polyvinylpyridine; polyvinylpyrrolidone; polyurethanes; salts thereof and copolymers thereof.

5 9. The injectable gel-forming composition as claimed in claim 6, characterized in that the crosslinked polymer(s) is (are) chosen from the crosslinked polymers of hydroxyethyl methacrylate, of hydroxypropyl methacrylate or of poly(N-acryloyl-2-amino-2-hydroxy-
10 methyl-1,3-propanediol), and also from the crosslinked copolymers of hydroxyethyl methacrylate and of poly(N-acryloyl-2-amino-2-hydroxymethyl-1,3-propanediol), or of hydroxypropyl methacrylate and of poly(N-acryloyl-2-amino-2-hydroxymethyl-1,3-propanediol).

15 10. The injectable gel-forming composition as claimed in any one of the preceding claims, characterized in that the degree of crosslinking of the crosslinked polymer is between 0.5 and 12% (m/V).

20 11. The injectable gel-forming composition as claimed in any one of the preceding claims, characterized in that the crosslinked polymer(s) represent(s) from 1 to 30% (m/V).

25 12. The injectable gel-forming composition according to any one of the preceding claims, characterized in that the size of the particles of crosslinked polymer(s) is between 1 and 1000 μm .

30 13. The injectable gel-forming composition as claimed in any one of the preceding claims, characterized in that it comprises at least one linear hydroxyethyl methacrylate or hydroxypropyl methacrylate polymer or a
35 linear hydroxyethyl methacrylate-based or hydroxypropyl methacrylate-based copolymer and particles of cross-linked polymers of hydroxyethyl methacrylate, of hydroxypropyl methacrylate or of poly(N-acryloyl-2-amino-2-hydroxymethyl-1,3-propanediol), and/or of

crosslinked copolymers of hydroxyethyl methacrylate and of poly(N-acryloyl-2-amino-2-hydroxymethyl-1,3-propanediol) or of hydroxypropyl methacrylate and of poly(N-acryloyl-2-amino-2-hydroxymethyl-1,3-propanediol).

5

14. The injectable gel-forming composition as claimed in claim 13, characterized in that it comprises:

- at least one linear, hydroxyethyl methacrylate-based or hydroxypropyl methacrylate-based copolymer, and
- 10 - at least particles of crosslinked copolymers of hydroxyethyl methacrylate or hydroxypropyl methacrylate and of poly(N-acryloyl-2-amino-2-hydroxymethyl-1,3-propanediol).

15 15. The injectable gel-forming composition as claimed in any one of the preceding claims, characterized in that the biocompatible, water-miscible solvent(s) is (are) chosen from N-methylpyrrolidone, dimethylethylamide, diethylene glycol dimethyl ether, ethyl lactate, 20 ethanol, dimethoxyethane, dimethylsulfoxide, glycofurool, and mixtures thereof.

16. The injectable gel-forming composition as claimed in claim 15, characterized in that said solvents are 25 chosen from ethanol and N-methylpyrrolidone.

17. The injectable gel-forming composition as claimed in any one of the preceding claims, characterized in that it also contains one or more adjuvants chosen from 30 dyes; imaging markers; anti-inflammatory agents; angiogenic agents; antimitotics; angiogenesis inhibitors; growth factors; vitamins; hormones; proteins; vaccines; peptides; antiseptics and antimicrobial agents.

35

18. An injectable gel-forming composition as defined in any one of claims 1 to 17, for its use in filling pipes and cavities.

19. An injectable gel-forming composition as defined in any one of claims 1 to 17, for its use for producing therapeutic vascular occlusions, for tissue reconstruction or the treatment of gastro-esophageal reflux or urinary incontinence, for percutaneous implantation,
5 or for reducing wrinkles.

20. A linear copolymer-based intermediate solution, characterized in that it comprises:

- 10 - at least one linear copolymer of hydroxypropyl methacrylate and of acrylonitrile, and/or at least one copolymer of hydroxypropyl methacrylate and of N-tert-butylacrylamide and/or at least one copolymer of hydroxypropyl methacrylate and of acetoacetoxyethyl
15 methacrylate, and
- at least one biocompatible, water-miscible solvent;
it being understood that, when said intermediate solution contains a linear copolymer of hydroxypropyl methacrylate and of acrylonitrile, then the solvent is
20 not dimethyl sulfoxide.